In response to the Final Restriction Requirement, Applicants amended claims 1-3 and replaced claims 6-8 with new claims 58-60, respectively, to delete non-elected subject matter from this application. Claims 31, 39, 43, 47, 49, 51 and 55 have been amended to correct the dependencies of these claims. Applicants wish to point out to the Examiner that claims that were dependant on claim 7 have been amended to be dependant on claim 58 (which corresponds to original claim 6) and therefore remain within the scope of the claimed invention. Applicants reserve the right to file a continuing application to pursue non-elected subject matter. No new matter has been added.

In response to the objection to the specification, Applicants have amended the specification to include proper trademark symbols and the generic terminology for trademark symbols.

In response to the claim rejections under 35 U.S.C. § 112, applicants have amended claims 40-41, 44-49, 52, 53, 56, and 57 to include proper trademark symbols and the generic terminology for trademark symbols.

Applicants have voluntarily amended claim 35 to better define applicants' invention.

A copy of the amended claims showing all the changes made therein is enclosed as attachment A.

If the Examiner should determine any fees are due, the Commissioner is authorized to deduct such fees from Deposit Account No. 19-0365.

Respectfully submitted,

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ATTACHMENT A

(Added material is underlined and deleted material is in brackets)

Please amend the paragraph beginning on line 25 of page 3 and ending on line 17, page 4 with the following rewritten paragraph:

IN THE SPECIFICATION

Additionally, one or more compounds of the present invention can be co-administered or used in combination with one or more disease-modifying antirheumatic drugs (DMARDS) such as methotrexate, azathioprine leflunomide, penicillamine, gold salts, mycophenolate mofetil, cyclophosphamide and other similar drugs. One or more compounds of the invention can also be co-administered with or used in combination with one or more NSAIDS such as piroxicam, naproxen, indomethacin, ibuprofen and the like; one or more COX-2 selective inhibitors such as Vioxx® (rofecoxib from Merck & Company, Whitehouse Station, NJ) and Celebrex® (celecoxib from Pfizer Inc., New York, New York); one or more COX-1 inhibitors such as Feldene® (Piroxicam from Pfizer Inc., New York, New York); immunosuppressives such as steroids, cyclosporine, Tacrolimus, rapamycin, muromonab-CD3 (OKT3), Basiliximab and the like; biological response modifiers (BRMs) such as Enbrel® (etanercept from Wyeth-Ayerst, Philadelphia, PA), Remicade® (infliximab from Centocor, Inc., Malvern, PA), IL-1 antagonists, anti-CD40, anti-CD28, IL-10, anti-adhesion molecules and the like; and other anti-inflammatory agents such as p38 kinase inhibitors, PDE4 inhibitors, TACE inhibitors, chemokine receptor antagonists, Thalidomide® (Celgene Corporation, Warren, NJ) and/or other small molecule inhibitors of pro-inflammatory cytokine production. One or more compounds of this invention can also be co-administered with or used in combination with one or more H1 antagonists such as Claritin® (loratadine from Schering-Plough Corporation, Kenilworth, NJ), Clarinex® (desloratadine from Schering-Plough Corporation, Kenilworth, NJ), Zyrtec®(cetirizine HCl from Pfizer Inc., New York,

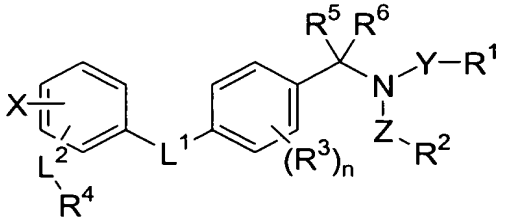
New York), Allegra® (fexofenadine from Aventis, Bridgewater, NJ), Benadryl® (diphenhydramine from Parke-Davis, Morris Plains, NJ), and other H1 antagonists. Other drugs that the compounds of the invention can be co-administered or used in combination with include Anaprox, Arava, Arthrotec, Azulfidine, Aspirin, Cataflam, Celestone Soluspan, Clinoril, Cortone Acetate, Cuprimine, Daypro, Decadron, Depen, Depo-Medrol, Disalcid, Dolobid, Naprosyn, Gengraf, Hydrocortone, Imuran, Indocin, Lodine, Motrin, Myochrysine, Nalfon, Naprelan, Neoral, Orudis, Oruvail, Pediapred, Plaquenil, Prelone, Relafen, Solu-Medrol, Tolectin, Trilisate and/or Volataren. These include any formulations of the above-named drugs.

For the treatment of multiple sclerosis, one or more compounds of the invention can be co-administered or used in combination with Avonex® (interferon beta-1a from Biogen, Cambridge, MA), Betaseron® (Interferon beta-1b from Chiron from Emeryville, CA) and/or Copaxone® (glatiramer acetate from Teva Pharmaceutical Industries, North Wales, PA).

IN THE CLAIMS

Please amend Claims 1-3, 31, 39-41, 43-49, 51-53, and 55-57 to read as follows.

1. A compound of the formula



or a pharmaceutically acceptable salt or solvate thereof; wherein:

R^1 is selected from the group consisting of H, alkyl, haloC_1-C_6 alkyl, cycloalkyl, cycloalkylNH-, arylalkyl, heterocycloalkyl, heteroaryl, -$N(R^2)_2$, -$N(R^2)$aryl, unsubstituted aryl and aryl substituted with one to three X, wherein each R^2 can be the same or different and is independently selected when there are more than one R^2 present;

R^2 is selected from the group consisting of H and C_1-C_6 alkyl;

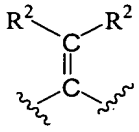
R^3 is 1-3 substituents selected from the group consisting of H, C_1-C_6 alkyl, Cl, F, CF_3, OCF_2H, OCF_3, OH and C_1-C_6 alkoxy, wherein R^3 can be the same or different and is independently selected when there are more than one R^3 present;

R^4 is selected from the group consisting of H, C_1-C_6 alkyl, C_1-C_6 alkoxy, cycloalkyl, alkenyl, aryl, benzyl, [heteroaryl, heterocycloalkyl,] arylNH-, [heteroarylNH-,] cycloalkylNH-, $N(R^2)_2$, or $N(R^2)$aryl, said alkyl, alkoxy, cycloalkyl, alkenyl, and phenyl, [pyridine-N-oxide and heteroaryl] optionally substituted with one to three X, wherein X can be the same or different and is independently selected when there are more than one X present;

R^5 is H or C_1-C_6 alkyl;

R^6 is H or C_1-C_6 alkyl; or

R^5 and R^6 taken together with the carbon atom to which they are attached form a carbonyl group;

L^1 is [ , -$C(R^2)_2$-, -C(O)-, -$CHOR^2$-, -$C{=}NOR^5$-,] -SO_2-, -SO-, or -S-[, -O-, -$N(R^2)$-, -$C(O)NR^2$-, -$N(R^2)C(O)$-, -$CHCF_2$- or -CF_2-];

L^2 is [a covalent bond, C_1-C_6 alkylene, -C $(R^2)_2$-,  , -$CHOR^2$-, -$C(R^2)$OH, -$C{=}NOR^5$-,] -SO_2-, [-$N(R^2)SO_2$-,] -SO-, or -S-[, -O-, -$SO_2N(R^2)$-, -$N(R^2)_2$-, -$C(O)N(R^2)$- or -$N(R^2)C(O)$-];

X is selected from the group consisting of H, halogen, CF_3, CN, OCF_2H, OCF_2CF_3, OCF_3, OR^2, C_1-C_6 alkyl, cycloalkyl, cycloalkoxy, C_1-C_6 alkoxy, alkoxyC_1-C_6 alkoxy, O-cycloalkyl, cycloalkylamino, cycloalkylalkoxy, heteroalkyl, -OSO_2R^2,
-$COOR^2$, -$CON(R^2)_2$, $N(R^2)_2$, and NR^2aryl, wherein X can be the same or different, and is independently selected when there are more than one X present;

Y is a covalent bond, -CH_2-, -SO_2-, or -C(O)-;

Z is a covalent bond, -CH_2-, -SO_2- or -C(O)-; or

Y, R^1, Z and R^2 can be taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl; with the following provisos:

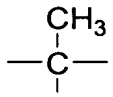
[L^2 and R^4, when taken together, cannot have two heteroatoms covalenty bonded together;]

when R^2 is H, Z cannot be -S(O)-, -SO_2-, or -C(O)-; and

when Y is a covalent bond, R^1 cannot form a N-N bond with the nitrogen atom.

2. A compound according to claim 1 wherein

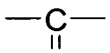
L^1 is -SO_2-, [-CH_2-, -$CHCH_3$-, -C(O)-, -C=NOR^5-, -$C(CH_3)_2$-, -CHOH-, -O-,] -S- or –S(O)-;

L^2 is -SO_2-[,-C(O)-, -CH_2-, -$CH(CH_3)$-,-$C(CH_3)_2$-,  , -NH-, -O-,  , -$NHSO_2$-, -NHC(O)-, or];

R^1 is H, -CH_3NH_2, -CH_2CF_3, -NHC_3H_7, -NHC_2H_6, -NHC_4H_9, C_1-C_6 alkyl,
-CF_3, -$CH(CH_2)_2$, thiophenyl, morpholinyl, cyclopropyl, benzyl, naphthyl, -$C(CH_3)_3$, NHphenyl, 3,5-difluorophenyl, phenyl, N-cyclopentyl or $N(CH_3)_2$;

R^2 is H or CH_3;

R^3 is OH;

R^4 is [furanyl, pyridyl, pyrimidyl,] thiophenyl, [quinolyl, t-butoxy,] alkoxyl, cyclohexyl, phenyl, tolyl, C_3H_7, [pyrimdyl,] methoxyphenyl[, morpholinylphenyl] or CH_3[; with the proviso that when R^4 is t-butoxy, L^2 must be -C(O)-, $-CH_2-$,  -$CHCH_3$-, -$C(CH_3)_2$-or ,]$_1$ all of the above optionally substituted with one to three X, wherein X can be the same or different and are independently selected when the are more than one X present;

R^5 and R^6 are independently H or CH_3;

Y is a covalent bond, $-SO_2-$ or -C(O)-;

Z is a covalent bond; or

R^1, Y, R^2 and Z taken together with the nitrogen atom form a morpholinyl group.

3. The compound according to claim 2 wherein

X is halogen, OH, or cyclopropyl;

R^3 is OH;

R^5 and R^6 are independently H or CH_3;

X is H, halogen, CF_3, OCH_3, OH, OCF_3, OCF_2H, CH_3 or C_1-C_6 cycloalkyl;

Y is a covalent bond;

Z is $-SO_2-$ or -C(O)-;

L^1 is $-SO_2-$ [or $-CH_2-$];

L^2 is $-SO_2-$;

R^1 is CH_3 or CF_3; and

R^4 is phenyl, [pyrimidyl or pyridyl,] said phenyl[, pyrimidyl or pyridyl groups] optionally substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, OH, CF_3 and halogen, wherein said substituents can be the same or different and are independently selected when there are more than one subsituent.

31. A pharmaceutical composition comprising one or more compounds according to claim [7] 58 and one or more pharmaceutically acceptable carriers.

35. The method of claim [32] 34 wherein the condition or disease treated is selected from the group consisting of rheumatoid arthritis, multiple sclerosis, seasonal allergic rhinitis and chronic obstructive pulmonary disease.

39. A method of treating rheumatoid arthritis which comprises co-administration one or more compounds selected from the class consisting of a COX-2 inhibitor, a COX-1 inhibitor, an immunosuppressive, a steroid, an anti-TNF-α compound, a PDE IV inhibitor or other classes of compounds indicated for the treatment of rheumatoid arthritis and one or more compounds of Claim [7] 58.

40. The method of Claim 38 wherein the COX-2 inhibitor is [Celebrex or Vioxx] celecoxib or rofecoxib, the COX-1 inhibitor is [Feldene] piroxicam, the immunosuppressive is methotrexate, leflunimide, sulfasalazine or cyclosporin, the steroid is β-methasone and the anti-TNF-α compound is [Enbrel or Remicade] etanercept or infliximab.

41. The method of Claim 39 wherein the COX-2 inhibitor is [Celebrex or Vioxx] celecoxib or rofecoxib, the COX-1 inhibitor is [Feldene] piroxicam, the immunosuppressive is methotrexate, leflunimide, sulfasalazine or cyclosporin, the steroid is β-methasone and the anti-TNF-α compound is [Enbrel or Remicade] etanercept or infliximab.

43. A composition for treating rheumatoid arthritis which comprises one or more compounds selected from the class consisting of a COX-2 inhibitor, a COX-1 inhibitor, an immunosuppressive, a steroid, an anti-TNF-α compound or other classes of compounds indicated for the treatment of rheumatoid arthritis and one or more compounds of Claim [7] 58.

44. The composition of Claim 42 wherein the COX-2 inhibitor is [Celebrex or Vioxx] celecoxib or rofecoxib, the COX-1 inhibitor is [Feldene] piroxicam, the immunosuppressive is methotrexate, leflunimide, sulfasalazine or cyclosporin, the steroid is β-methasone and the anti-TNF-α compound is [Enbrel or Remicade] etanercept or infliximab.

45. The composition of Claim 43 wherein the COX-2 inhibitor is [Celebrex or Vioxx] celecoxib or rofecoxib, the COX-1 inhibitor is [Feldene] piroxicam, the immunosuppressive is methotrexate, leflunimide, sulfasalazine or cyclosporin, the steroid is β-methasone and the anti-TNF-α compound is [Enbrel or Remicade] etanercept or infliximab.

46. A method of treating multiple sclerosis which comprises co-administration one or more compounds selected from [Avonex, Betaseron, Copaxone] interferon beta-1a, interferon beta-1b, glatiramer acetate or other compounds indicated for the treatment of multiple sclerosis and one or more compounds of Claim 1.

47. A method of treating multiple sclerosis which comprises co-administration one or more compounds selected from [Avonex, Betaseron, Copaxone] interferon beta-1a, Interferon beta-1b, glatiramer acetate or other compounds indicated for the treatment of multiple sclerosis and one or more compounds of Claim [7] 58.

48. A composition for treating multiple sclerosis which comprises one or more compounds selected from [Avonex, Betaseron, Copaxone] interferon beta-1a, interferon beta-1b, glatiramer acetate or other compounds indicated for the treatment of multiple sclerosis and one or more compounds of Claim 1.

49. A composition for treating multiple sclerosis which comprises one or more compounds selected from [Avonex, Betaseron, Copaxone] interferon beta-1a, Interferon beta-1b, glatiramer acetate or other compounds indicated for the treatment of multiple sclerosis and one or more compounds of Claim [7] 58.

51. A method of treating psoriasis which comprises co-administration of one or more compounds selected from the class consisting of an immunosuppressive, a steroid, an anti-TNF-α compound or other classes of compounds indicated for the treatment of psoriasis and one or more compounds of Claim [7] 58.

52. The method of Claim 50 wherein the immunosuppressive is methotrexate, leflunimide, sulfasalazine or cyclosporin, the steroid is β-methasone and the anti-TNF-α compound is [Enbrel or Remicade] etanercept or infliximab.

53. The method of Claim 51 wherein the immunosuppressive is methotrexate, leflunimide, sulfasalazine or cyclosporin, the steroid is β-

methasone and the anti-TNF-α compound is [Enbrel or Remicade] etanercept or infliximab.

55. A composition for treating psoriasis which comprises one or more compounds selected from the class consisting of an immunosuppressive, a steroid, an anti-TNF-α compound or other classes of compounds indicated for the treatment of psoriasis and one or more compounds of Claim [7] 58.

56. The composition of Claim 54 wherein the immunosuppressive is methotrexate, leflunimide, sulfasalazine or cyclosporin, the steroid is β-methasone and the anti-TNF-α compound is [Enbrel or Remicade] etanercept or infliximab.

57. The composition of Claim 55 wherein the immunosuppressive is methotrexate, leflunimide, sulfasalazine or cyclosporin, the steroid is β-methasone and the anti-TNF-α compound [Enbrel or Remicade] etanercept or infliximab.